UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 10/631,874 | 07/31/2003 | Indranil Nandi | G-33302P1 | 1795 |

1095 7590 04/21/2006

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

| EXAMINER | |
|---|---|
| HENRY, MICHAEL C | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1623 | |

DATE MAILED: 04/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/631,874 | NANDI ET AL. | |
| | Examiner | Art Unit | |
| | Michael C. Henry | 1623 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *23 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

The following office action is a responsive to the Amendment filed, 09/23/05.

The amendment filed 09/23/05 affects the application, 10/631,874 as follows:

1. Claims 1, 18 and 19 have been amended. This leaves claims 1-20.

2. The responsive to applicants' amendments is contained herein below.

### *Claim Rejections - 35 USC § 103*

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Domet et al. (US 4,929,605) in combination with Nakajima et al. (JP 09315971 A2, September 12, 1997).

In claim 1, applicant claims "A pharmaceutical composition consisting essentially of fexofenadine or a pharmaceutical acceptable acid addition salt thereof, about 10 wt. % to about 70 wt. % of lactose, and about 1 wt. % to about 40 wt. % of a low-substituted hydroxypropyl cellulose, wherein the weight percents are based on the total weight of the pharmaceutical composition." Dependent claims 2,6-9, 12, 13 are drawn to specific wt. % and mg of the components of said composition. Claims 14-17 are drawn to low-substituted hydroxypropyl cellulose of specific average particle sizes and wt. %.

Domet et al. disclose a pharmaceutical composition in solid unit dosage form containing a therapeutically effective amount of a piperidinoalkanol compound, such as fexofenadine and

terfenadine, or a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable nonionic or cationic surfactant, and a pharmaceutically acceptable carbonate salt. Furthermore, Domet et al. disclose that said piperidinoalkanol derivatives (compounds) which are antihistamines, antiallergic agents and bronchodilators, are in general, only minimally soluble in water and therefore the therapeutically inactive ingredients in a pharmaceutical composition containing one or more of these compounds are very important in providing for their efficient and immediate absorption and bioavailability after oral administration (see col. 1, lines 11-33). It should be noted that piperidinoalkanol compounds fexofenadine and terfenadine, which are useful as antihistamines, antiallergic agents and bronchodilators are quite similar in structure, differing only by a substituent (i.e. methyl group as opposed to a carboxyl group).

The difference between applicant's claimed composition and the composition disclosed by Domet et al. is that applicant's composition contains lactose and low-substituted hydroxypropyl cellulose.

Nakajima et al. disclose a pharmaceutical composition consisting essentially of terfenadine, about 27 wt. % of lactose, and about 10 wt. % of a low-substituted hydroxypropyl cellulose, wherein the weight percents are based on the total weight of the pharmaceutical composition (see abstract, English Translation, Example/[0010]). Furthermore, Nakajima et al. disclose that terfenadine, is a piperidinoalkanol derivative-based antiallergic drug and that various preparations have been studied in an effort to improve the efficient and instantaneous absorption of terfenadine after oral administration, as well as its bioavailability. In addition, Nakajima et al disclose that their terfenadine-containing tablet preparation which is are prepared

by combining terfenadine with specific components in specific proportions, readily disintegrate, and the terfenadine contained therein is released favorably (see page 3, [0001-0003].

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made, in view of Domet et al. and Nakajima et al., to have prepared a pharmaceutical composition comprising fexofenadine, lactose and low-substituted hydroxypropyl cellulose to be used as an antihistamine composition, since Domet et al. disclose that there is a need for the immediate absorption and bioavailability of piperidinoalkanol compounds (derivatives) including fexofenadine and terfenadine (after oral administration) and Nakajima et al. disclose that specific components such as lactose and low-substituted hydroxypropyl cellulose improves the bioavailability (i.e. rapid disintegration and favorable release) of terfenadine.

One having ordinary skill in the art would have been motivated in view of Domet et al. and Nakajima et al., to have prepared a pharmaceutical composition comprising fexofenadine, lactose and low-substituted hydroxypropyl cellulose to be used as an antihistamine composition, since Domet et al. disclose that there is a need for the immediate absorption and bioavailability of piperidinoalkanol compounds (derivatives) including fexofenadine and terfenadine (after oral administration) and Nakajima et al. disclose that specific components such as lactose and low-substituted hydroxypropyl cellulose improves the bioavailability (i.e. rapid disintegration and favorable release) of terfenadine. It should be noted that the use of specific quantities (e.g., mg), wt. % and type of low-substituted hydroxypropyl cellulose of said composition depends on the need, such as the individual to which this composition is administered.

Claims 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakajima et al. (JP 09315971 A2, September 12, 1997) in combination with Domet et al. (US 4,929,605).

In claim 18, applicant claims "A method of preparing a pharmaceutical composition consisting essentially of fexofenadine or a pharmaceutical acceptable acid addition salt thereof, about 10 wt. % to about 70 wt. % of lactose, and about 1 wt. % to about 40 wt. % of a low-substituted hydroxypropyl cellulose, wherein the weight percents are based on the total weight of the pharmaceutical composition, said method comprising:

(a) mixing fexofenadine, lactose, low-substituted hydroxypropyl cellulose, and optionally one or more excipients to form a premix;

(b) adding a solvent and optionally a surfactant to the premix formed in Step (a) to form a wet granulation; and

(c) drying the wet granulation to form dried granules;

(d) optionally milling the dried granules; and

(e) mixing at least one excipient with the dried granules to form a pharmaceutical composition." Claim 19 is drawn to a method of preparing a pharmaceutical composition consisting essentially of fexofenadine or a pharmaceutical acceptable acid addition salt thereof, about 10 wt. % to about 70 wt. % of lactose, and about 1 wt. % to about 40 wt. % of a low-substituted hydroxypropyl cellulose, wherein the weight percents are based on the total weight of the pharmaceutical composition, said method comprising: ..... (d) optionally milling the dried granules; and ..... Claim 20 is drawn to the method according to claim 19 wherein the low shear mill is a conical screen.

Nakajima et al. disclose applicant's method of preparing a pharmaceutical composition comprising terfenadine, lactose, and a low-substituted hydroxypropyl cellulose, said method comprising: (a) mixing terfenadine, lactose, low-substituted hydroxypropyl cellulose, and other excipients to form a premix; (b) adding a solvent (purified water) to form a wet mixture; and (c) drying the wet mixture; (d) milling the dried mixture; and (e) mixing an excipient (magnesium stearate) with the dried mixture to form a pharmaceutical composition (see abstract, English Translation, Example/[0010]). It should be noted that the examiner considers the dried mixture to be granules or in granular form, since Nakajima et al. disclose that the mixture was sieved and regulated for particle size (see abstract, English Translation, Example/[0010]). Furthermore, Nakajima et al. disclose that terfenadine, is a piperidinoalkanol derivative-based antiallergic drug and that various preparations have been studied in an effort to improve the efficient and instantaneous absorption of terfenadine after oral administration, as well as its bioavailability. In addition, Nakajima et al disclose that their terfenadine-containing tablet preparation which is are prepared by combining terfenadine with specific components in specific proportions, readily disintegrate, and the terfenadine contained therein is released favorably (see page 3, [0001-0003].

The difference between applicant's method and the method disclosed by Nakajima et al. is that applicant's uses fexofenadine and not terfenadine and applicant does not disclose the use of a try dryer to form dried granules. However, the use of a specific type of dryer should not affect the composition formed and said use depends on factors like availability and or need.

Domet et al. disclose a pharmaceutical composition in solid unit dosage form containing a therapeutically effective amount of a piperidinoalkanol compound, such as fexofenadine and

terfenadine, or a pharmaceutically acceptable salt thereof, a pharmaceutically acceptable nonionic or cationic surfactant, and a pharmaceutically acceptable carbonate salt. Furthermore, Domet et al. disclose that said piperidinoalkanol derivatives (compounds) which are antihistamines, antiallergic agents and bronchodilators, are in general, only minimally soluble in water and therefore the therapeutically inactive ingredients in a pharmaceutical composition containing one or more of these compounds are very important in providing for their efficient and immediate absorption and bioavailability after oral administration (see col. 1, lines 11-33). It should be noted that piperidinoalkanol compounds fexofenadine and terfenadine, which are useful as antihistamines, antiallergic agents and bronchodilators are quite similar in structure, differing only by a substituent (i.e. methyl group as opposed to a carboxyl group).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made, in view of Nakajima et al. and Domet et al., to have used the method of Nakajima et al. to prepare a pharmaceutical composition comprising fexofenadine, lactose and low-substituted hydroxypropyl cellulose to be used as an antihistamine composition, since Domet et al. disclose that there is a need for the immediate absorption and bioavailability of piperidinoalkanol compounds (derivatives) including fexofenadine and terfenadine (after oral administration) and Nakajima et al. disclose that specific components such as lactose and low-substituted hydroxypropyl cellulose improves the bioavailability (i.e. rapid disintegration and favorable release) of terfenadine.

One having ordinary skill in the art would have been motivated in view of Nakajima et al. and Domet et al., to have used the method of Nakajima et al. to prepare a pharmaceutical composition comprising fexofenadine, lactose and low-substituted hydroxypropyl cellulose to be

used as an antihistamine composition, since Domet et al. disclose that there is a need for the immediate absorption and bioavailability of piperidinoalkanol compounds (derivatives) including fexofenadine and terfenadine (after oral administration) and Nakajima et al. disclose that specific components such as lactose and low-substituted hydroxypropyl cellulose improves the bioavailability (i.e. rapid disintegration and favorable release) of terfenadine. It should be noted that the use of specific quantities (e.g., mg), wt. % and type of low-substituted hydroxypropyl cellulose of said composition depends on the need, such as the individual to which this composition is administered. In addition, the use of specific mills such as a low shear mill is commonly used in the art in the preparation of such oral tablet formulations, and is well with the purview of a skill artisan does not appear to alter the said composition formed.

***Response to Amendment***

Applicant's arguments with respect to claims 1-20 have been considered but are moot in view of the new ground(s) of rejection.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652. The examiner can normally be reached on 8:30 am to 5:00 pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang, Ph.D can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 308-1235.

Michael C. Henry

Shaojia Anna Jiang, Ph.D.
Supervisory Patent Examiner
Art Unit 1623

April 13, 2006.